Armed Forces College of Medicine

AFCM

Synthetic opioids

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INTENDED LEARNING OBJECTIVES (ILO)

By the end of this lecture the student will be able to:

1. Explain the mechanism of action of MEPERIDINE
2. Identify the pharmacokinetics & therapeutic uses of MEPERIDINE
3. Identify the mechanism of action, therapeutic uses and adverse effects of FENTANYL
4. Identify the pharmacological characteristics and therapeutic uses of METHADONE
5. Identify the pharmacological actions of TRAMADOL

Main points:

- Mechanism of action and uses of meperidine. The drug causes less respiratory depression than morphine
- Fentanyl and its therapeutic uses. The drug is 80 times stronger than morphine.
- Methadone has an important role in treatment of morphine poisoning.
- Tramadol is an opioid agonist on mu receptors

Meperidine (Pethidine)

- *Meperidine* [me-PER-i-deen] is a synthetic opioid structurally unrelated to *morphine*. It is used for acute pain.
- **1. Mechanism of action:** *Meperidine* binds to opioid receptors, particularly μ receptors. It also binds well to κ receptors.

- **2. Actions:** *Meperidine* causes a depression of respiration LESS to that of *morphine*, but it has no significant cardiovascular action when given orally. On IV administration, *meperidine* produces a decrease in peripheral resistance and an increase in peripheral blood flow, and it may cause an increase in cardiac rate.
- Has an atropine like effect.

- **3- Pharmacokinetics:** *Meperidine* is well absorbed from the GI tract, and is available for oral administration 50%. However, *meperidine* is most often administered parenterally. The drug has a duration of action of 2 to 4 hours, which is shorter than that of *morphine*
- May cause seizures due to accumulation of metabolites (Normeperidine), so its use becomes less.

- **<u>Therapeutic Uses</u>:** 50 – 100 mg Orally or I.M.
  - 1- Severe Visceral pain e.g. Myocardial infarction.
  - 2- Alone in Biliary & Renal colic.
  - 3- Pre-anesthetic medication (Better than Morphine).
  - 4- Obstetric Analgesia: Meperidine + Hyoscine → Twilight Sleep → Less Fetal RC

Quiz

- Meperidine is used in obstetric analgesia in the following combination:
  a. Meperidine + Naloxone
  b. Meperidine + Atropine
  c. Meperidine + Loperamide
  d. Meperidine + Hyoscine
  e. Meperidine + Nalbuphine

  The Answer is D: Meperidine + Hyoscine

Fentanyl (Synthetic)

- 1- Derivative of *Meperidine*.
- 2- **Strong** μ-Agonist → **Strong** Analgesic → **80** Times > Morphine
- 3- *High Lipid solubility*: I.V. → Rapid Onset + Short duration (Redistribution)
- 4- Used as *I.V. Anesthesia*:
  - a- Fentanyl alone, *But* → Vomiting.
  - b- Fentanyl + Droperidol (Major tranquillizer) → *Neurolept- Analgesia*
  - c- Fentanyl + Droperidol + Nitrous oxide → *Neurolept-Anesthesia*
  - *NB) The emetic effect of Fentanyl is # Anti-emetic effect of Droperidol.*
- 5- *Adverse Effects* → Vomiting, Marked RC & Muscle tone → Trunkal rigidity

N.B.: Droperidol is a dopamine antagonist: blocks dopamine receptors in the CTZ, TTT of nausea & vomiting

Quiz

- A 52 years old woman presented with intense pain due to cancer breast, and metastasis in bone. The physician decided to initiate pain control with Fentanyl. One of the following proves the right decision taken by the physician:
  a. Fentanyl prevents vomiting caused by chemotherapy
  b. Is a strong mμ agonist, 80 times stronger than morphine
  c. Is a strong delta agonist 180 times stronger than morphine
  d. Can be added to diazepam to produce neurolept analgesia
  e. Acts on GABA receptors

The answer is B: Fentanyl is 80 times stronger than morphine

Methadone

- 1- *As* potent as Morphine.
- 2- *Better* Oral Bioavailability.
- 3- *Longer* $t_{½}$ = 1 – 2 days
- 4- *Local* anesthetic effect.
- 5- *Uses*:
  - a- Analgesic in Severe visceral pain e.g. Terminal cancer.
  - b- To substitute Morphine & Heroin during their withdrawal.
  - Tolerance & physical dependance develop more slowly with methadone than with morphine.

Tramadol

- Weak or μ receptor agonist.
- Analgesic effect → ↑ Opiate receptors & ↓ Uptake of Noradrenaline & Serotonin.
- Side effects: Fatigue, postural hypotension, seizures, difficulty in breathing, sleeping disorders, blurred vision.

- Which of the following is CORRECT regarding tramadol?
  a. Is an opioid antagonist
  b. Is a mixed agonist-antagonist on opioid receptors
  c. Is an opioid agonist on mu receptors
  d. Increases uptake of Dopamine and Noradrenaline
  e. Decreases uptake of Dopamine & Noradrenaline

  The Answer is C: Is an opioid agonist on mu receptors

To Summarize

- Mechanism of action, therapeutic uses and side effects of Meperidine, Fentanyl, Tramadol were discussed.

SUGGESTED TEXTBOOKS

1. Whalen, K., Finkel, R., & Panavelil, T. A. (2018) Lippincott's Illustrated Reviews: Pharmacology (7th edition.). Philadelphia: Wolters Kluwer

2. Katzung BG, Trevor AJ. (2018). Basic & Clinical Pharmacology (14th edition) New York: McGraw-Hill Medical.